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Study No.: S3B10934					
Title: An Open-Label, Non-Randomized, Single-Dose Study of the Pharmacokinetics of Alosetron 1mg in Adolescents 12-17 Years of Age With Non-Constipated Irritable Bowel Syndrome					
Rationale: Based on the prevalence of irritable bowel syndrome (IBS) in children and adolescents, it was anticipated that alosetron might be used in the pediatric population, and might provide a meaningful therapeutic benefit for this group. Data on the use of alosetron in a pediatric population had to be obtained in order to support safe pediatric use of alosetron. This study was conducted in order to provide pharmacokinetic data on alosetron in adolescents 12 to 17 years of age. This study will also examined the safety and tolerability of alosetron in adolescents.					
Phase: I					
Study Period: 16 Feb 2000 to 30 Nov 2000					
Study Design: This was a single-dose, open-label, non-randomized study. The duration of the study was up to approximately 4 weeks per subject.					
Centres: Four sites in the United States					
Indication: Non-Constipated Irritable Bowel Syndrome (IBS) in Adolescents 12-17 Years Of Age.					
Treatment: A single oral 1mg dose tablet containing 1mg alosetron as the hydrochloride salt (GR68755C).					
Objectives: The primary objective of this study was to determine the systemic exposure after a 1mg dose of alosetron administered to adolescent subjects aged 12 to 17 years.					
Statistical Methods: Twenty-four subjects were planned to be enrolled in the study (12 females, and 12 males). Since this was an observational study, it was anticipated that 24 subjects would have provided an adequate assessment of the pharmacokinetics (PK) of alosetron in adolescents. The smaller sample size (n=21) was still considered adequate for the performance of formal statistical analyses.					
Pharmacokinetic Analysis: Serum alosetron concentrations at each time point, and PK parameters (area under the plasma concentration-time curve from time 0 to infinity [AUC _∞], maximum observed plasma concentration [C _{max}], time of observed maximum concentration [t _{max}], and drug half-life [t _{1/2}]) were summarized using descriptive statistics. For the geometric mean of each PK parameter, 95% confidence intervals (CI) were constructed. Data are presented for all subjects by gender and age group.					
This study was terminated prior to achieving the planned enrollment of 24 subjects. A total of 21 subjects (12 females and 9 males) were enrolled and all completed the study. Subjects were divided in age groups: 12-13, 14-15 and 16-17 years, each group containing 4 females and 4 males except for the 16 to 17 year age group, which consisted of 4 females and 1 male.					
The early termination of the study occurred as the result of a decision by Glaxo Wellcome (GW) on 28 November 2000, to discontinue the alosetron clinical development program. Following this decision, GW immediately initiated an orderly cessation of all ongoing trials.					
Study Population: Male and female subjects aged 12 to 17 years with non-constipated IBS as defined by the Rome criteria for IBS. Females of child-bearing potential were to be using a GW acceptable method of contraception and to have demonstrated a negative pregnancy test prior to study drug administration.					
Number of Subjects:			Alosetron 1mg		
Planned, N			24		
Dosed, N			21		
Completed, n (%)			21 (100)		
Total Number Subjects Withdrawn, N (%)			0		
Withdrawn Due to Adverse Events, n (%)			0		
Withdrawn Due to Lack of Efficacy, n (%)			0		
Withdrawn for Other Reasons, n (%)			0		
Demographics:	Age 12-13	Age 14-15	Age 16-17	Females	Males
N (Safety)	8	8	5	12	9
Females:Males	4:4	4:4	4:1	12:0	0:9
Mean Age in Years (SD)	12.5 (0.5)	14.6 (0.5)	16.6 (0.5)	14.5 (1.9)	14.0 (1.5)

Mean Weight in kg (SD)	50.36 (12.55)	70.14 (14.99)	54.58 (7.88)	60.75 (16.07)	56.43 (14.47)
Caucasian, n (%)	6 (75)	7 (88)	5 (100)	12 (100)	6 (67)
Alosetron PK Parameters Following a Single 1mg Oral Dose					
PK Parameter	Age 12-13 N=8	Age 14-15 N=8	Age 16-17 N=5	Females N=12	Males N=9
AUC _∞ (ng•h/mL)					
Geo. Mean	15.7	21.5	12.2	19.6	13.4
95% CI	9.72, 25.3	12.7, 36.6	3.47, 42.8	12.70, 30.3	7.60, 23.7
C _{max} (ng/mL)					
Geo. Mean	5.19	7.47	3.84	6.36	4.63
95% CI	3.22, 8.37	4.93, 11.3	1.26, 11.7	4.35, 9.32	2.66, 8.05
t _{max} (h)					
Est. Median	1.51	1.02	1.53	1.50	1.02
Min-Max	1.00-4.00	1.00-2.00	0.98-1.75	0.98-4.00	1.00-2.03
t _{1/2}					
Geo. Mean	1.37	1.22	1.43	1.46	1.16
95% CI	1.12, 1.67	0.884, 1.69	0.983, 2.09	1.22, 1.75	0.919, 1.47
Safety Results: The safety population consisted of all subjects who receive a dose of the study medication.					
Adverse Events:	Age 12-13	Age 14-15	Age 16-17	Females	Males
N (Safety)	8	8	5	12	9
Subjects With AEs, n (%)	4 (50)	2 (25)	4 (80)	7 (58)	3 (33)
Abdominal Discomfort & Pain	1 (13)	0	2 (40)	2 (17)	1 (11)
Gastrointestinal Discomfort & Pain	0	2 (25)	0	2 (17)	0
Headache	1 (13)	1 (13)	1 (20)	3 (25)	0
Injection Site or Infusion Reaction	0	0	2 (40)	1 (8)	1 (11)
Serious Adverse Events (SAEs), n (%) [# considered by the investigator to be related, possibly related, or probably related to study medication]:					
Subjects With SAEs, n (%)	0	0	0	0	0

Publications:

No publications.

Date Updated: 11-May-2005